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31. AUG. 1992
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Attorney Work Product

May 29, 1992

Dr. James L. Charles
Philip Morris U.S.A.
4201 Commerce Road
P.O. Box 26583
Richmond, Virginia 23261-6583

Dear Jim:

Enclosed are copies of the most recent draft mid-tier white papers authored by your company and revised by Covington & Burling. As you know, these draft papers recently were circulated to several scientific consultants for comment. In accordance with their comments, we request that you review and revise the enclosed papers to assure that each one includes a thorough discussion of

- the specific function(s) the additive serves in cigarettes, and
- the probable exposure to a smoker, given the fate of the additive and its effect on the composition of cigarette smoke (e.g., transfer and retention rates and pyrolysis products).

Please discuss both published and unpublished data pertinent to these issues.

In addition, please make revisions to respond to the specific issues identified below.

1. Ammonium Bicarbonate

- In the physical properties table at page 3, there is a blank space across from the term, "volatile". Should that space be filled? Yes

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- The discussion of chronic animal studies at pages 6-7 cites the finding of the Select Committee on GRAS Substances that ammonium carbonate produced no tumors in rabbits at specified doses. Were any signs of toxicity reported? yes - but in chronic studies the endpoint of interest is carcinogens.
- The discussion of the Wanatabe (1978) study at pages 7-8 in which IV injections of ammonium bicarbonate were administered to cats, dosages are stated only in mmol/kg. Please state the dose in mg/kg, if possible.

2. Propylparaben (propyl-para-hydroxybenzoate)

- Please list references for all endnote numbers appearing in the text.
- Please clarify the relationship between the listed references and the bibliography (other papers provide only references).
- Please provide information on the basic physical and chemical properties of propylparaben (melting point, boiling point, etc.).
- In the discussion of metabolism at page 4, the paper states, "propylparaben undergoes conjugation and is excreted primarily in the urine." Please explain with what chemical(s) propylparaben conjugates.
- In the discussion of acute animal studies at page 7, please explain your use of the phrase, "acutely lethal dose."
- In the discussion of acute animal studies at page 8, the paper explains that dogs dosed by IV injection experienced no adverse central nervous system (CNS) effects. Please explain why CNS effects apparently were expected.

3. Potassium Citrate

- In the background discussion at page 3, the paper asserts that potassium citrate

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has been used for purposes of smoking cessation. Please explain the rationale and mechanism for this treatment.

- Because the industry maximum use level for potassium citrate has not been established, please provide a brief discussion of the customary amount of the additive that is used to achieve the functional effect(s) (e.g., in terms of percentage of cigarette tobacco by weight).

The current draft papers have been typed into our wordprocessing system. Therefore, you may provide your revisions in the form of typed texts to be inserted into or substituted for the text of the current draft papers. If you wish to delete text from the current papers or make other modest revisions, you may simply mark the text of the enclosed draft papers.

Please return the revised draft mid-tier white papers to us no later than August 15, 1992. Your prompt response will help us to prepare for possible ingredient activity by HHS or Congress next year.

Best regards.

Very truly yours,

Sarah E. Taylor/zf

Sarah E. Taylor

Enclosures

cc: Stanley Temko
Clausen Ely

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